

RESEARCH ARTICLE

# Lower cognitive baseline scores predict cognitive training success after 6 months in healthy older adults: Results of an online RCT

Mandy Roheger<sup>1,2</sup>  | Elke Kalbe<sup>1</sup> | Anne Corbett<sup>3</sup>  | Helen Brooker<sup>3</sup>  | Clive Ballard<sup>3</sup> 

<sup>1</sup>Department of Medical Psychology, Neuropsychology and Gender Studies & Center for Neuropsychological Diagnostics and Intervention (CeNDI), University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany

<sup>2</sup>Department of Neurology, University Medicine Greifswald, Greifswald, Germany

<sup>3</sup>Institute of Health Research, University of Exeter Medical School, University of Exeter, Exeter, UK

## Correspondence

E. Kalbe; Department of Medical Psychology | Neuropsychology and Gender Studies & Center for Neuropsychological Diagnostics and Intervention (CeNDI), University of Cologne, Faculty of Medicine and University Hospital Cologne, Kerpener Str. 68, 50937 Cologne, Germany.  
Email: elke.kalbe@uk-koeln.de

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## Abstract

**Background:** Identifying predictors for general cognitive training (GCT) success in healthy older adults has many potential uses, including aiding intervention and improving individual dementia risk prediction, which are of high importance in health care. However, the factors that predict training improvements and the temporal course of predictors (eg, do the same prognostic factors predict training success after a short training period, such as 6 weeks, as well as after a longer training period, such as 6 months?) are largely unknown.

**Methods:** Data (N = 4,184 healthy older individuals) from two arms (GCT vs. control) of a three-arm randomized controlled trial were reanalyzed to investigate predictors of GCT success in five cognitive tasks (grammatical reasoning, spatial working memory, digit vigilance, paired association learning, and verbal learning) at three time points (after 6 weeks, 3 months, and 6 months of training). Possible investigated predictors were sociodemographic variables, depressive symptoms, number of training sessions, cognitive baseline values, and all interaction terms (group\*predictor).

**Results:** Being female was predictive for improvement in grammatical reasoning at 6 weeks in the GCT group, and lower cognitive baseline scores were predictive for improvement in spatial working memory and verbal learning at 6 months.

**Conclusion:** Our data indicate that predictors seem to change over time; remarkably, lower baseline performance at study entry is only a significant predictor at 6 months training. Possible reasons for these results are discussed in relation to the compensation hypothesis.

## KEYWORDS

cognitive training, compensation account, healthy older adults, prediction

## 1 | INTRODUCTION

A serious problem faced by the growing older population is cognitive decline and the coherent loss of independence.<sup>1</sup> Yet, several systematic

reviews and meta-analyses show that the training of cognitive abilities can help to improve and maintain cognitive function in the healthy aging process.<sup>2,3</sup> Given the accumulating evidence for the effectiveness of cognitive training and the importance of considering individual differences in

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training response,<sup>4</sup> few studies have addressed the question of who benefits most from cognitive training interventions. Possible prognostic factors for improvements after a cognitive training are sociodemographic factors, cognitive abilities at entry to the training, genetic parameters, blood factors, and personality traits.<sup>5</sup> Furthermore, results seem inconsistent: some studies state that higher age is a positive predictor for cognitive training success in healthy older adults,<sup>5,6</sup> whereas others indicate that younger individuals benefit more from training.<sup>7,8</sup> A recent systematic review on prognostic factors of changes after memory training in healthy older individuals showed that the tendency of the prognostic factor (the more of x/the more of y vs. the more of x/the less of y) is dependent on the used dependent outcome measure of the studies (eg, whether post-test scores or changes scores were used in calculations as the dependent variable). The use of these different dependent variables has led to seemingly contradictory results regarding prognostic factors for training success in the current literature.<sup>9</sup> After systemizing the included studies according to their dependent variables, the authors were able to draw the preliminary conclusion that older adults seem to benefit more from memory training than younger adults, when using the change scores (post minus pre-performance) as the dependent variable, answering the specific question: "Who benefits from the training?". Yet, the review also emphasizes the need for elaborated prognostic factor studies with large sample sizes, clear descriptions of prognostic factor and confounder measurements, and clear reporting standards in the field of nonpharmacological interventions to shed further light on this important topic.

A further, under-investigated aspect of prognostic factor research on cognitive training success in healthy older adults is the temporal course of the prognostic factors: Do the same prognostic factors predict training success after a short training period (eg, 6 weeks), as well as after longer periods (eg, 6 months or even 1 year)? However, it is also important to consider the difference between predictors of training success of studies that provide an intervention for a specific time frame (eg, 6 weeks<sup>10</sup>) and then investigate predictors for cognitive function at follow-up times in contrast to studies in which the participants have ongoing training, and predictors are investigated at different measurement periods throughout this training. To the knowledge of the authors, no study has focused on the latter aspect.

Therefore, the present paper investigates who benefits from an online general cognitive training (GCT) intervention in healthy older adults by identifying predictors of the ongoing training intervention at 6 weeks, 3 months, and 6 months. For that purpose, data from an already published RCT were reanalyzed.<sup>11</sup>

## 2 | METHODS

### 2.1 | Study design

Data were taken from a double-blind 6-month online randomized three-arm controlled trial with healthy older adults. In a previous paper, short- and long-term effects of this RCT were reported,<sup>11</sup> showing that GCT and reasoning cognitive training (ReaCT) conferred a benefit to self-reported instrumental activities of daily living scores

### Key Points

- Prediction analysis of  $n = 4,185$  healthy older adults revealed that sex and cognitive baseline performance were significant predictors of changes when performing a GCT.
- There is a time course underlying significant predictors for changes when performing a GCT: female sex was predictive for gains in grammatical reasoning after 6 weeks of training, and cognitive baseline level at study entry was predictive for GCT gains in tests for spatial working memory and verbal recall after 6 months, but not after 6 weeks or 3 months of training.

as well as reasoning and verbal learning at 6 months. In the present study, only data from the GCT and the active control group (CG) were used, but with four measurement times at baseline, 6 weeks, 3 months, and 6 months. The present study only focused on the evaluation of predictors of changes after GCT, as the GCT targets multiple cognitive domains and, therefore, differs substantially in its concept from the ReaCT, which targets primary executive functions. The CGT resembles most cognitive trainings which are offered to older people in the context of prevention of cognitive decline. Thus, the identification of predictors of GCT is of high relevance. Even though, predictors of changes after ReaCT are also of interest, their analyses and discussions lay beyond the scope of the present paper. The St. Thomas' Hospital Research Ethics Committee granted approval (Ref: 09/H0802/85) for the study and the study was registered on the International Standard Randomised Controlled Trial Number (ISRCTN) clinical trial database (Ref: ISRCTN72895114).

### 2.2 | Participants

Eligible participants for the study were individuals older than 50 years of age with access to a computer and the internet. Through a partnership with the British Broadcasting Corporation (BBC), Alzheimer's Society (UK), and the Medical Research Council, all adults older than 50 years in the United Kingdom and internationally were invited to take part in this online RCT. Interested older individuals were invited to register and consent through a secure connection and an ethically approved online process to the study. Participants then received their own login details and were randomized to a study group (GCT, ReaCT, or CG). Throughout the intervention, participants received reminder emails to continue their training and complete their online cognitive assessments.

### 2.3 | General cognitive training

In the present study, only data from participants of the GCT compared to an active CG were investigated. Participants were recommended to

**TABLE 1** Training sessions included in the general cognitive training packages

Training session	Task	Main outcome measure
Attention 1	Click on rapidly appearing symbols as quickly as possible, but only if it matched one of the "target" symbols presented at the top of the screen.	Total number of correct trials across the two runs.
Attention 2	Select numbers in order from the lowest to the highest from a series of slowly moving, rotating, numbers.	Total number of correct trials across the two runs.
Memory 1	State the number of remaining items of baggage left in an airport x-ray machine after watching a sequence of items moving down a conveyer belt toward the machine. The number of bags going in did not equal the number of bags coming out.	Number of problems completed in 3 min.
Memory 2	Identify matching pairs of picture cards after being shown the images and the cards being flipped over.	Total number of correct trials across the two runs.
Maths	Complete simple math sums (eg, 17-9) as quickly as possible.	Total number of correct trials across the two runs.
Visuospatial	Find the missing piece from a jigsaw puzzle by selecting from six alternatives.	Total number of correct trials across the two runs.

Note: This table was modified based on Corbett et al.<sup>11</sup>

train for 10 minutes daily, even though flexibility in training duration was allowed. The GCT consisted of six cognitive tasks that trained attention, memory, mathematics, and visuospatial abilities. An overview of the tasks is provided in Table 1. The CG performed online tasks involving a game in which people were asked to put a series of statements in the correct numerical order.

## 2.4 | Outcome measures

Investigated outcome measures were completed at four time points: at baseline (after registering for the trial and before starting the first training session; T1), at 6 weeks (T2), 3 months (T3), and 6 months (T4). Data were collected from all participants irrespective of the number of completed training sessions.

Outcome measures were changes in grammatical reasoning, spatial working memory, digit vigilance, verbal short-term memory, and verbal learning. Grammatical reasoning was measured using the total number of trials answered correctly in 90 seconds minus the number answered incorrectly in the Baddeley grammatical reasoning test.<sup>12</sup> Spatial working memory was measured with the widely used spatial working memory test<sup>13</sup> in which participants searched a series of on-screen boxes to find a hidden symbol. The main outcome was the change in the score of the average number of boxes in the successfully completed trials. Digit vigilance was measured through a version of the "digit span" task, in which each successful trial is followed by a digit span that is one digit longer than the last one, and each unsuccessful trial is followed by a digit span one digit shorter than the last. The main outcome measure was the average number of digits in all successfully completed trials. The paired associates test<sup>14</sup> was used to measure verbal short-term memory. In the test participants see a series of objects, one at a time, and select the correct location of each object in "windows" they had previously been shown. The main outcome measure was the average number of completed correct object-place associations in the trials. Verbal learning was measured by changes in the recognition score on the revised Hopkin's Verbal Learning Test.<sup>15</sup> The test is comprised of six alternate forms, each containing 12 nouns and 4 words, which are taken each from one of three semantic categories to be learned over the course of three learning trials. This is followed by a recognition trial 20 to 25 minutes later composed of 24 words, including the 12 target words and 12 false positives.

## 2.5 | Predictors

The possible predictors of age, sex, education, ethnicity, group, baseline cognitive scores, depression, and number of intervention sessions as well as all their interactions (group\*predictor) were assessed. Age (numerical variable, in years), sex (assessed as a binary variable: male vs. female), education (categorized in five categories: none, primary school, secondary school, further education, and university graduate), ethnicity (categorized in seven categories: Asian, Black, Middle Eastern, mixed White/Black, mixed White/Asian, White, and other), and depression (assessed as numerical variable on the Personal Health Questionnaire) were assessed before the training started. For all tests used as outcome measures, baseline performance scores (T1) were included as possible predictors (meaning that, for example, for the outcome "improvement in grammatical reasoning," the predictor "baseline grammatical reasoning score" was included). The predictor "group" was dichotomized (GCT vs. CG). The number of training sessions was assessed as the total number of training sessions a participant completed until the time of measurement. Predictor assessment was blinded.

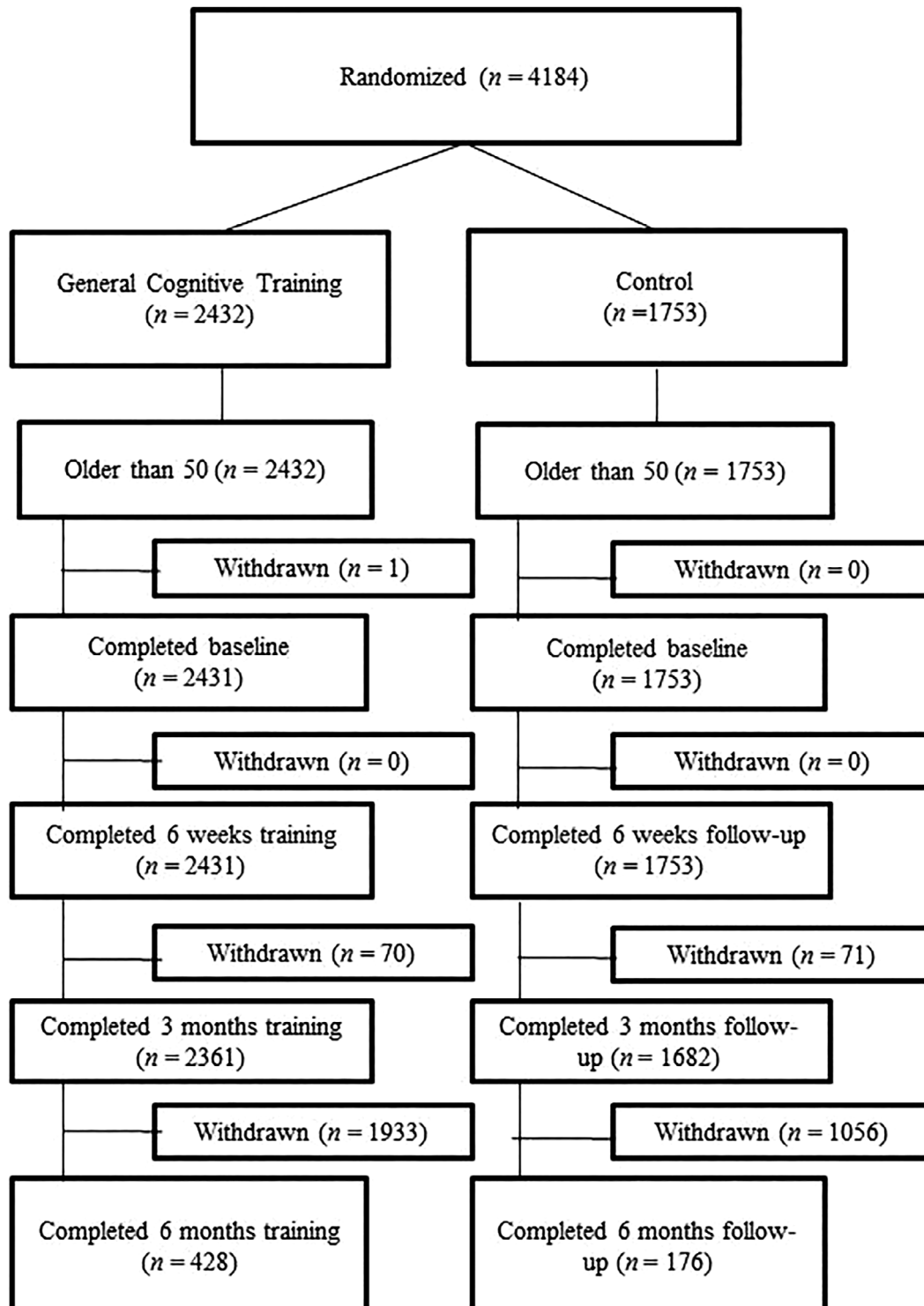
## 2.6 | Statistical analyses

Statistical analyses were performed using R.<sup>16</sup> For all statistical comparisons, the significance level was set at  $\alpha=.05$ . Descriptive statistics

are displayed with means and SDs for numerical variables, all other values are displayed in n(%) and were calculated using *t*-tests or chi-square tests, where appropriate.

We calculated predictions of cognitive improvement for the GCT group at three different time points: 6 weeks (T2), 3 months (T3), and 6 months (T4). When measuring training gain in CT studies, it is

important to consider which dependent variable should be used.<sup>17</sup> Instead of taking absolute scores, that is the posttest scores (performance after training) as dependent variables in the regression, which would answer the question “Is *x* a likely cause of *y*,” we decided to take change scores as the dependent variable. Change scores provide answers to our main question “Whose score is most likely to increase/



**FIGURE 1** Participant flow throughout the study

decrease over time?"<sup>18</sup> Yet, change scores are suitable as a way of measuring change, even though they do not consider differences in relative improvement across persons.<sup>19</sup>

Multiple regressions were calculated using the change scores (T2 minus T1; T3 minus T1; T4 minus T1) of grammatical reasoning, spatial working memory, digit vigilance, paired associative learning, and verbal recall as dependent variables. The following predictors were integrated simultaneously with the enter method: Baseline score of dependent variable (T1), group (GCT vs. CG), age, sex, ethnic origin, education, depression, number of training sessions, and all interactions between all predictors with the group. Effect sizes are displayed in the beta weights of the regression, for which  $\beta > .1$  indicates a small effect,  $\beta > .3$  a medium effect, and  $\beta > .5$  indicates a large effect.<sup>20</sup> We are particularly interested in the results of the interaction terms (group\*predictors), as these indicate significant predictors only for the

GCT group compared with the CG. For sensitivity analysis, all multiple regression analyses were also conducted only with the sample size of the 6 months sample ( $n = 604$ ).

### 3 | RESULTS

#### 3.1 | Demographic characteristics of the sample at all three measurements

A total of 2,432 participants was included in the GCT group at baseline and 1,753 participants were included in the CG at baseline. Figure 1 shows a flow chart of the participants throughout the study. Table 2 presents the demographic characteristics of the GCT group and the CG at baseline, 6 weeks, 3 months, and 6 months. No

**TABLE 2** Descriptive statistics of the GCT and the CG at baseline, 6 wk, 3 mo, and 6 mo follow-ups

Characteristics	Participants who completed baseline and 6-wk follow-ups ( $n = 4,184$ )			Participants who completed 3-mo follow-up ( $n = 4,043$ )			Participants who completed 6-mo follow-up ( $n = 604$ )		
	GCT $n = 2,431$	Control $n = 1,753$	<i>P</i> value	GCT $n = 2,361$	Control $n = 1,682$	<i>P</i> value	GCT $n = 428$	Control $n = 176$	<i>P</i> value
Age, y	59.1 (6.4)	59.1 (6.6)	.689	59.1 (6.4)	59.1 (6.6)	.988	60.19 (6.60)	60.81 (7.24)	.312
Sex, female	1676 (68.9)	1093 (62.4)	.195	1036 (62.0)	1036 (68.8)	.198	321 (75.0)	98 (55.7)	.345
Ethnic origin			.233			.238			.369
Asian	31 (1.3)	10 (0.6)		28 (1.2)	9 (0.5)		4 (0.9)	1 (0.6)	
Black	4 (0.2)	4 (0.2)		3 (0.1)	4 (0.2)		0 (0.0)	1 (0.6)	
Middle Eastern	7 (0.3)	4 (0.2)		7 (0.3)	3 (0.2)		0 (0.0)	0 (0.0)	
Mixed White/ Black	1 (0.04)	8 (0.5)		1 (0.0)	8 (0.5)		0 (0.0)	0 (0.0)	
Mixed White/ Asian	9 (0.4)	11 (0.6)		8 (0.1)	11 (0.7)		1 (0.2)	1 (0.6)	
White	2359 (97)	1707 (97.4)		2281 (97.1)	1628 (97.4)		420 (98.1)	172 (97.7)	
Other	19 (0.8)	9 (0.5)		19 (0.8)	9 (0.5)		1 (0.2)	1 (0.6)	
Education			.307			.300			.408
None	55 (2.3)	37 (2.1)		52 (2.2)	34 (2.0)		6 (1.4)	2 (1.1)	
Primary school	10 (0.4)	9 (0.5)		10 (0.4)	9 (0.5)		1 (0.2)	2 (1.1)	
Secondary school	418 (17.2)	320 (18.3)		404 (17.2)	297 (17.8)		67 (15.7)	37 (21.0)	
Further education	717 (29.5)	556 (31.7)		692 (29.5)	531 (31.8)		123 (28.7)	61 (34.7)	
University graduate	1230 (50.6)	831 (47.4)		1189 (50.6)	801 (47.9)		229 (53.5)	74 (42.0)	
Baddeley grammatical reasoning test	14.1 (5.4)	14.1 (5.3)	.744	14.1 (5.3)	14.2 (5.2)	.543	13.70 (5.43)	13.71 (5.24)	.981
SWM test	4.9 (1.3)	5.0 (1.2)	.138	4.9 (1.3)	4.9 (1.2)	.136	4.96 (1.25)	4.91 (1.22)	.700
Paired associates learning test	3.5 (0.6)	3.5 (0.6)	.409	3.5 (0.6)	3.5 (0.6)	.341	3.50 (0.59)	3.42 (0.60)	.119
Digit Span ladder test	4.8 (1.1)	4.7 (1.1)	.198	4.8 (1.1)	4.7 (1.1)	.312	4.67 (1.13)	4.63 (1.11)	.660

Note: Age (in y), Baddeley grammatical reasoning test, SWM test, paired associates learning test, and Digit Span ladder test are reported with means and SDs. All other values are  $n$  (%). *P* values indicate group differences between the two groups at each of the three time points. Group differences were calculated using *t* tests and chi-square tests, where appropriate.

Abbreviations: GCT, general cognitive training; SWM, spatial working memory.

**TABLE 3** Predictors of general cognitive training success at 6 wk, 3 mo, and 6 mo follow-ups

Predictors	6 wk (n = 4,184) Dependent variables:					3 mo (n = 4,043) Dependent variables:					6 mo (n = 604) Dependent variables:				
	GR	SWM	DV	PAL	VL	GR	SWM	DV	PAL	VL	GR	SWM	DV	PAL	VL
Intercept	12.33***	3.89***	3.84***	3.46***	6.10***	12.51***	3.89***	3.98***	3.76***	0.57	13.18***	4.60***	4.04***	3.44***	2.29***
Group	0.99	0.12	0.04	-0.03	0.64	0.70	0.12	0.13	0.10	0.82	0.86	0.77+	0.12	0.35	-0.12
Time 1	-0.48***	-0.65***	-0.57***	-0.73***	-1.12***	-0.48***	-0.65***	-0.63***	-0.73***	-1.00***	-0.48***	-0.56***	-0.63***	-0.80***	-0.81
Age	-0.07***	-0.01	-0.01**	-0.01***	-0.03+	-0.07***	-0.00	-0.01*	-0.01***	0.00	-0.07+	-0.02*	-0.01	-0.01	0.01
Sex	-0.17	-0.09	-0.15**	-0.03	0.26+	0.06	-0.08	-0.08+	0.02	0.26+	0.13	-0.03	-0.10	0.04	-0.19
Education	-0.28***	-0.03*	-0.04**	-0.03*	-0.01	-0.27***	-0.03*	-0.04**	-0.01	0.07+	-0.29+	-0.29+	-0.04	-0.02	0.03
Ethnic	0.08+	0.01	-0.01	-0.16+	0.04	-0.08*	0.01	0.00	-0.04	0.17	-0.09	-0.04	0.03	0.02	-0.06
Depression	-0.00+	0.00	-0.00	-0.00	0.00	-0.00**	0.00	-0.00	-0.02***	0.02	0.02	0.01	-0.02	0.01	0.03
Number of training sessions	0.00	-0.00	0.00	-0.00	-0.02+	0.00	-0.00	-0.00	-0.00	-0.00	0.00	-0.00	0.00	-0.00	0.00
Time 1*Group	0.01	-0.01	-0.04**	0.00	0.01	0.01	-0.01	-0.02	0.00	0.04	-0.00	-0.10**	-0.06	0.03	-0.16*
Age*Group	-0.01	-0.00	0.00	-0.00	-0.00	-0.01	-0.00	-0.00	-0.00	-0.01	-0.00	-0.00	0.00	-0.01+	0.01
Sex*Group	0.26*	0.04	0.05+	0.00	-0.07	0.14	0.04	0.04	-0.01	-0.13	0.01	0.01	0.05	-0.00	0.03
Education*Group	0.04	0.01	0.02*	0.01	-0.01	0.02	0.01	0.01	-0.00	-0.02	0.01	-0.00	-0.01	0.01	-0.03
Ethnic*Group	-0.11	0.01	0.03	0.00	-0.06	-0.01	0.01	0.00	0.04*	-0.15*	-0.09	0.08	0.02	-0.02	0.14
Depression*Group	0.00*	-0.00*	0.00	0.00	0.00	0.00+	-0.00*	-0.00	0.01**	-0.01	0.01	0.00	0.01	-0.00	-0.02
Number of training sessions*Group	-0.00*	0.00**	-0.00	0.00	0.00	-0.00+	0.00**	0.00	0.00	0.00	0.00	0.00	-0.00	-0.00	-0.00
Adjusted R <sup>2</sup>	0.26***	0.34***	0.31***	0.37***	0.32***	0.26***	0.34***	0.32***	0.36***	0.43***	0.33***	0.47***	0.40***	0.37***	0.40***

Note: All participants older than 50 years were included (general cognitive training and control group). Reference groups: control group, male sex, white ethnicity, and university graduate.

Abbreviations: DV, digit vigilance; GR, grammatical reasoning; PAL, paired associate learning; SWM, spatial working memory; VL, verbal learning.

Significant codes: \*\*\* = 0.001; \*\* = 0.01; \* = 0.05; "+", "n" = 0.1.

**TABLE 4** A simplified overview of the significant interaction terms in the multiple regressions at 6 wk, 3 mo, and 6 mo

Predictors	General cognitive training				
	Grammatical reasoning	Spatial working memory	Digit vigilance	Paired associate learning	Verbal learning
6 wk					
Baseline					
Age					
Sex	Being female ↑				
Education					
Ethnic					
Depression					
Number of training sessions					
3 mo					
Baseline					
Age					
Sex					
Education					
Ethnic					
Depression					
Number of training sessions					
6 mo					
Baseline		↓			↓
Age					
Sex					
Education					
Ethnic					
Depression					
Number of training sessions					

Note: Only significant interaction terms with an effect size that indicates at least a small effect ( $\beta \geq .10$ ) are reported. ↓/↑ = indicate a small effect,  $\beta > .01$ . ↓↓/↑↑ = indicate a medium effect,  $\beta > .03$ . ↓↓↓/↑↑↑ = indicate a large effect,  $\beta > .01$ .

statistical differences were found between the two groups at any time point, except for the number of training or game sessions: the CG ( $M = 41.46$ ;  $SD = 92.790$ ) trained significantly less than the experimental group ( $M = 53.64$ ,  $SD = 84.259$ ;  $t(4183) = -4.423$ ;  $P = .000$ ).

### 3.2 | Predictors of cognitive training success at all three measurements

An overview of the results of the prediction analyses of all three time points (6 weeks, 3 months, and 6 months) is provided in Table 3. Furthermore, a simplified overview of the significant interaction terms (indicating significant predictors for the GCT compared to the CG) and their effect sizes are depicted in Table 4. Only significant interaction terms with an effect size that indicates at least a small effect ( $\beta \geq .10$ ) are reported in Table 4.

At 6 weeks measurement (T2), results showed that for grammatical reasoning, higher scores in the GCT group were predicted by female sex ( $\beta = .26$ ), indicating a small effect. No significant interaction terms were seen when investigating spatial working memory, digit

vigilance, paired association learning, and verbal learning, which had an effect size of  $\beta \geq .1$ .

At 3 months measurement (T3), results indicated no significant interaction terms for any of the investigated dependent variables.

At 6 months measurement (T4), however, lower baseline performances in the GCT group predicted higher scores in spatial working memory ( $\beta = -.10$ ) and in paired association learning ( $\beta = -.16$ ), both indicating a small effect. No significant interaction predictors for grammatical reasoning, digit vigilance, and verbal learning were seen at T4.

## 4 | DISCUSSION

The aim of the present paper was to identify predictors for GCT success in healthy older adults of an ongoing online GCT at 6 weeks, 3 months, and 6 months. Our main results are that (a) sex and cognitive baseline performance were significant predictors of training success and (b) there is a time course underlying these predictors. More specifically, we found that female sex was predictive for gains in grammatical reasoning after 6 weeks of training, but not after 3 or 6 months



of training. Furthermore, our results indicate that cognitive baseline level at study entry was predictive for GCT gains in tests for spatial working memory and verbal recall after 6 months, but not after 6 weeks or 3 months of training.

Regarding predictors of training success, the fact that being female was a significant predictor for gains in a verbal task, measuring grammatical reasoning (though only after 6 weeks) of GCT, is remarkable. To date, sex differences in cognitive training interventions have rarely been studied in healthy older adults. However, one other study with older participants with mild cognitive impairment found that women showed stronger improvements in verbal tasks (immediate and delayed verbal episodic memory and verbal working memory) after a 6-week multidomain cognitive training program.<sup>21</sup> Notably, meta-analytic data demonstrate that healthy women perform better than men on tests of verbal learning and memory,<sup>22</sup> and women also outperform men in syntactic complexity and grammatical diversity.<sup>23</sup> Taken together, the data might point to “sex-specific plasticity,” and more particular, stronger plasticity for verbal tasks in women.<sup>24</sup>

Furthermore, a low cognitive baseline level at study entry was a significant predictor for gains in the GCT group (only at 6 months) in spatial working memory and verbal learning. This finding is in line with several other studies that found lower cognitive baseline level at study entry to be predictive of cognitive training improvement.<sup>10,25</sup> The compensation hypothesis<sup>26</sup> may account for this pattern; it implies that healthy older adults who are already functioning at optimal levels have less room for improvement in GCT performance, whereas those with low function may improve to a greater degree.

Regarding the time pattern of prediction of training success, our study showed that being female is only predictive for improvement in grammatical reasoning at the 6-week measurement, but not after 3 or 6 months of training. Yet, it may be possible that women might be more capable than men of activating their former resources in verbal domains immediately at the beginning of the training,<sup>24</sup> meaning that verbal resources are stronger in women and enable a faster activation of knowledge and strategies in this domain but that this sex-specific advantage diminishes over time. However, this aspect will have to be further investigated in future studies.

We also found that lower cognitive baseline performance at study entry is only a significant predictor after 6 months of training, but not earlier in the course of the training. This may be interpreted based on how participants profit in a comparable way during a longer period of time independently of their baseline level, but after 6 months, participating in a GCT is more successful for individuals starting with lower baseline performance. One explanation is that individuals with higher cognitive baseline levels reach their limit earlier, whereas those with a lower cognitive baseline level have a longer time period in which they may improve. It is important to note that in the literature, several studies have found that cognitive test performance at study entry is also predictive for gains after shorter periods of 6 to 10 weeks of cognitive training<sup>10,27,28</sup>—results that contradict our findings. Possible reasons for this inconsistency remain speculative but could lie in the use of different cognitive trainings or statistical methods (eg, the inclusion of the CG in the multiple regression in our study). However, a comparison of our study

with other training studies is also difficult because our data refer to an ongoing training with an ongoing training also at follow-up measurements, whereas most other studies have a specific training duration (eg, two times a week<sup>10</sup>) and predictors of training success then refer to post-intervention (which would be comparable to our prediction analysis after a shorter period of time, for example, 6 weeks) or follow-up examination after a period of no training (which we do not have). In more detail, instead of a classical pre-intervention-post-FU design used in most studies in which no training is conducted between post-test and FU, the present study had several measurement points (at 6 weeks, 3 months, and 6 months) in which the intervention was still ongoing (pre-test - intervention—6 week measurement—intervention—3 month measurement—intervention—6 months measurement—intervention).

Results showed that the CG trained significantly less than the intervention group, indicating a possible loss of motivation to participate in the study. As we did not collect data on training motivation, reasons for this remain speculative. Participants in the CG may not have enjoyed the offered games or may not have had the feeling of efficiency. Future studies need to ensure an active control group that has equally challenging and interesting tasks compared to the intervention group.

Particular strengths of the present paper are the fact that it reports on the first study to investigate predictors of cognitive training success over the time course in a large sample taken from an RCT. Yet, as a possible limitation, it has to be kept in mind that the sample may be biased due to the fact that often highly educated and highly motivated participants conduct cognitive trainings,<sup>29</sup> although this is a more general problem of cognitive training studies per se. A further limitation of the present analyses is the fact that training dose was only measured in terms of “number of training sessions” instead of “total training time.” Notably, training time could vary across individuals, as some people might have trained only a few times but for longer periods or vice versa. Therefore, results include a possible over- or underestimation of the effect of training dose. Unfortunately, training time was not registered in the current trial. Future studies should measure individuals' total training time, especially when individuals have the power to decide their training time per session on their own to avoid such bias. As a further limitation, we did not correct for multiple testing (eg, by using the Bonferroni correction) due to the fact that it was an exploratory study investigating the time course of possible predictors for changes after memory training. Yet, we only discussed predictors with high effect sizes ( $>.1$ ). However, future studies should imply corrections for multiple testing to confirm the found results.

## 5 | CONCLUSION

To conclude, our study showed that sex and cognitive variables may predict GCT success and there seems to be a differential time course for this prediction. As patterns of training success prediction might help to tailor cognitive trainings to individuals with different profiles, research should further unravel prediction patterns and their underlying mechanisms. Ultimately, this research might help to optimize the prevention of cognitive decline in a personalized medicine approach.



## CONFLICT OF INTEREST

The authors do not declare any conflicts of interests.

## DATA AVAILABILITY STATEMENT

Research data are not shared.

## ORCID

Mandy Roheger  <https://orcid.org/0000-0002-6015-3194>

Anne Corbett  <https://orcid.org/0000-0003-2015-0316>

Helen Brooker  <https://orcid.org/0000-0002-7908-263X>

Clive Ballard  <https://orcid.org/0000-0003-0022-5632>

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